

R E M A R K S

The Examiner is respectfully requested to acknowledge receipt of the certified copies of the priority documents that were filed August 20, 2001.

The Examiner is also respectfully requested to return initialed copies of the form PTO/SB/08A dated December 3, 2002 and the forms PTO/SB/08A and PTO/SB/08B filed on June 20, 2003.

Claims 3, 5 and 6 were editorially revised. Enclosed is a MARKED-UP VERSION OF THE AMENDMENTS TO THE CLAIMS.

New claims 20 and 21 are supported by the original Claim 1.

The presently claimed invention concerns a muscular fatigue-controlling composition which comprises a muscular fatigue-controlling effective amount of (a) an imidazole compound which is anserine or a salt thereof and (b) D-ribose, as active ingredients, in combination with an excipient.

The presently claimed invention also is directed to a method for providing a muscular fatigue-controlling effect comprising orally administering to a person in need thereof a muscular fatigue-controlling effective amount of a muscular fatigue-controlling composition which comprises (a) an imidazole compound which is anserine or a salt thereof and (b) D-ribose, as active ingredients.

Claims 1 and 6 were rejected under 35 USC 102 as being anticipated by Hageman et al. (USP 6,420,342) for the reasons set

forth at the bottom of page 2 of the Office Action.

Hageman et al. disclose a nutritional composition which is stated to be useful for the prevention or treatment of various diseases. The Hageman et al. composition comprises ribose and folate as essential components. In column 13, line 20-35 of Hageman et al., a composition containing ribose, folic acid and yeast extract is disclosed. It was stated in the Office Action that yeast extract inherently contains anserine, referring to column 8, lines 29-35 of USP 4,028,184 to Ishiyama et al.

The several conditions and diseases described in column 5, lines 39-52 of Hageman et al. (such as trauma; surgery; inflammation; subfertility; laceration problems; gut disorders; jaundice; cancer; arthritis; vascular problems; ischaemia; aging; respiratory infections; impaired immune function; burns; sepsis; malnutrition; malaria; cystic fibrosis; migraine; neurological problems including Huntington's disease, Parkinson's disease, Alzheimer's disease, schizophrenia and depression; and pain) do not include a muscular fatigue-controlling effect, which is recited in applicants' claims.

It is initially noted that applicants' claims do not recite folate which is required by Hageman et al.

It is respectfully submitted that column 8, line 29-35 of USP 4,028,184 does not explicitly state that yeast extract contains anserine. Column 8, lines 29-35 of USP 4,028,184 refers only to "derivatives" of "compounds" (such derivatives being

carnosine or anserine) and "natural substances" (such as yeast extract) containing such "compounds". Column 8, lines 29-35 of USP 4,028,184 does not state that yeast extract contains anserine.

Submitted concomitantly herewith is a DECLARATION UNDER 37 CFR 1.132 of Yoshiharu MATAHIRA dated June 25, 2003. In Test Example 1 of the June 25, 2003 MATAHIRA DECLARATION, it is confirmed that yeast extract does not contain anserine. It is respectfully submitted that this showing proves that the statement in the Office Action that yeast extract contains anserine is incorrect.

In summary, Hageman et al. do not disclose control of muscular fatigue; and Hageman et al. and USP 4,028,184 do not disclose the combination of anserine and D-ribose, as recited in applicants' claims.

Claims 1, 3, 5 to 7 and 11 to 16 were rejected under 35 USC 103 as being unpatentable over Harris et al. (USP 5,965,596) in view of St. Cyr et al. (USP 6, 159,942) for the reasons set forth beginning at the middle of page 3 of the Office Action and continuing to the middle of page 4 of the Office Action.

It was admitted in the Office Action that Harris et al. do not teach the inclusion of ribose.

The method disclosed in Harris et al. is directed to administering beta-alanine along with L-histidine and/or creatine, orally or by injection, to increase the contents of

beta-alanine alone or increasing the content of beta-alanine with L-histidine and/or creatine in blood plasma, thereby increasing the synthesis of beta-alanylhistidine dipeptide and creatine. Namely, Harris et al. disclose increasing the anaerobic working capacity of muscles and other tissues by increasing the beta-alanylhistidine content in blood plasma. However, Harris et al. give no specific description concerning the ingestion of anserine.

On page 3 of the Office Action, the following is stated:

"Harris teaches administration of chicken broth, which contains anserine and carnosine, to subjects (example 2). Harris et al teaches the additional use of creatine and carbohydrates, such as sugar, in the composition (claims)."

However, chicken broth contains not only anserine and carnosine, but creatine, collagen, amino acid and vegetables for flavor. The Office Action does not state that there is a sufficient amount of anserine in chicken broth to provide a muscular fatigue-controlling effect. Although Harris et al disclosed simple carbohydrates, "ribose" is not specifically mentioned. Accordingly, there are many possible combinations of various sugars and various components in chicken broth. It is respectfully submitted that one having ordinary skill in the art could not predict with any degree of certainty that out of such many combinations, that applicants' combination of anserine and ribose would provide a synergistic effect.

St. Cyr et al. describe that by administering a pentose, ATP

synthesis is accelerated, and the energy useful for mammals can be increased. By the administration of only ribose, the synthesis of ATP can be accelerated, but the consumption rate of ATP cannot be improved. In this regard, in Test Example 2 of the enclosed June 25, 2003 MATAHIRA DECLARATION, it is shown that anserine activates the ATPase in muscles and increases the consumption rate of ATP as the energy source. Namely, when anserine and ribose are used in combination, not only ATP synthesis is accelerated by ribose, but also the consumption rate of ATP is increased by anserine, and resultingly, energy can be remarkably increased. Accordingly, this fact proves that anserine and ribose exhibit a synergistic effect with respect to providing a muscular fatigue-controlling effect. The above described synergistic effect provided by anserine and ribose was first discovered by the present inventors.

Regarding the "Response to Arguments" at the middle of page 4 of the Office Action, the Examiner is requested to clarify the meaning of the terminology of "statistical evaluation". Does this terminology mean that numerical values should have been indicated? However, in the previous Declaration Under 37 CFR 1.132 of Yoshiharu Matahira dated September 30, 2002 the amounts of the active ingredients are adjusted to be the same level, and the swimming time of the anserine/ribose mixture-administered group is remarkably prolonged (Fig. 1). If the effect is "an additive effect", when the total amounts of the active

ingredient(s) are the same, the effects would have been expected to be at the same level. However, by the combination of anserine and ribose, although the total amounts of the active ingredient(s) are at the same level as the others, the swimming time is remarkably prolonged. It is submitted that such an effect is "a synergistic effect".

It is therefore respectfully submitted that applicants' claimed invention is not anticipated by the references.

It is further respectfully submitted that the applicants' claimed invention is not rendered obvious over the references, either taken singly or combined in the manner relied upon in the Office Action in view of the distinctions discussed hereinabove. It is moreover submitted that there are no teachings in the references to combine them in such a manner relied upon in the Office Action.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



Richard S. Barth
Reg. No. 28,180

Frishauf, Holtz, Goodman & Chick, P.C.

767 Third Ave., 25th Floor

New York, NY 10017-2023

Tel. No. (212) 319-4900

Fax No.: (212) 319-5101

RSB/bg

Enc.: (1) PETITION FOR EXTENSION

(2) MARKED-UP VERSIONS OF THE AMENDMENTS TO THE CLAIMS

(3) DECLARATION UNDER 37 CFR 1.132 of Yoshiharu MATAHIRA



MARKED-UP VERSION OF THE AMENDMENT TO THE CLAIMS
(SERIAL NO. 09/933,438)

3. (Amended) The [antifatigue] composition according to Claim 1, wherein the imidazole compound is contained in an amount of at least 10 mass%.

5. (Twice Amended) The [antifatigue] composition according to Claim 1, wherein the imidazole compound is contained in an amount of from 5 to 50 mass% and the D-ribose is contained in an amount of from 5 to 50 mass%.

6. (Twice Amended) The [antifatigue] composition according to Claim 1, wherein the composition further comprises at least one substance selected from the group consisting of taurine, creatine, vitamin E, vitamin C, carotenoid, reduced glutathione and minerals.